Application No.: Filing Date:

December 19, 2000

nev Docket No.: SALK1720-6

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Amendments to the Specification

Please replace the previous Sequence Listing with the new Sequence Listing submitted herewith

Please replace the paragraph beginning at page 11, line 6 with the following replacement paragraph.

Presently preferred amino acid sequences encoding receptor proteins of the invention include the sequence set forth in Sequence ID No. 2 (which represents a mouse activin receptor amino acid sequence), a modified form of Sequence ID No. 2 wherein the arginine at residue number 39 is replaced by a lysine, the isoleucine at residue number 92 is replaced by a valine, and the glutamic acid at residue number 288 is replaced by a glutamine (which modified form of Sequence ID No. 21 is referred to hereinafter as Sequence ID No. 1611", and represents a human activin receptor amino acid sequence), the sequence set forth as Sequence ID No. 4 (which represents a Xenopus activin receptor amino acid sequence), and Sequence ID No. 12 (which represents a rat activin receptorlike kinase amino acid sequence) as well as functional, modified forms thereof. Those of skill in the art recognize that numerous residues of the above-described sequences can be substituted with other, chemically, sterically and/or electronically similar residues without substantially altering the biological activity of the resulting receptor species

Please replace the paragraph beginning at page 11, line 28 with the following replacement paragraph

In accordance with another embodiment of the present invention, there is provided a soluble, extracellular, ligand-binding protein, further characterized by:

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having sufficient binding affinity for at least one member of the activin/TGF- β superfamily of polypeptide growth factors such that concentrations of ≤ 10 nM of said polypeptide growth factor occupy $\geq 50\%$ of the binding sites on said receptor protein, and

having at least about 30% sequence identity with respect to:

the sequence of amino acids 20-134 set forth in Sequence ID No.

2;

the sequence of amino acids 20-134 set forth in Sequence ID No.

16 2, wherein the arginine residue at position number 39 is replaced by a lysine, and the isoleucine at residue number 92 is replaced by a valine:

the sequence of amino acids 21-132 set forth in 10 Sequence ID

No. 4; or

the sequence of amino acids 26-113 set forth in Sequence ID No.

12

Please replace the paragraph beginning at page 12, line 14 with the following replacement paragraph.

---Presently preferred soluble, extracellular, ligand-binding proteins contemplated by the present invention can be further characterized by having at least about 50% sequence identity with respect to:

the sequence of amino acids 20-134 set forth in Sequence ID No.

2;

the sequence of amino acids 20-134 set forth in Sequence ID No.

16 2, wherein the arginine residue at position number 39 is replaced by a lysine, and the isoleucine at residue number 92 is replaced by a valine:

the sequence of amino acids 21-132 set forth in Sequence ID No.

4; or

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the sequence of amino acids 26-113 set forth in Sequence ID No.

12:

with the presently most preferred soluble, extracellular, 30 ligand-binding proteins having at least about 80% sequence identity with respect to the abovereferenced fragments of Sequence ID Nos. 2, 4 or 12.

Please replace the paragraph beginning at page 13, line 27 with the following replacement paragraph.

Especially preferred soluble, extracellular, ligand-binding proteins of the invention are those having substantially the same amino acid sequence as that set forth as:

residues 20-134 of Sequence ID No. 2;

residues 20-134 of Sequence ID No. 16 2, wherein the arginine residue at position number 39 is replaced by a lysine, and the isoleucine at residue number 92 is replaced by a valine:

residues 21-132 of Sequence ID No. 4; or residues 26-113 of Sequence ID No. 12. F-

Please replace the paragraph beginning at page 15, line 24 with the following replacement paragraph.

--The above-described receptor(s) can be encoded by numerous DNA sequences, e.g., a DNA sequence having a contiguous nucleotide sequence substantially the same as:

nucleotides 128 - 1609 of Sequence ID No. 1 (which encodes a mouse activin receptor);

variations of nucleotides 128 - 1609 of Sequence ID No. 15 1. wherein the codon for residue number 39 of the encoded amino acid codes for lysine, the codon for residue number 92 of the encoded amino acid codes for valine, and the codon f or residue number 288 of

4

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> the encoded amino acid encodes glutamine (which encodes a human activin receptor):

> nucleotides 528 - 1997 of Sequence ID No. 3 (which encodes a Xenopus activin receptor);

nucleotides 147-1550 of Sequence ID No. 11 (which encodes a rat activin receptor); or

variations of any of the above sequences which encode the same amino acid sequences, but employ different codons for some of the amino acids. --

Please replace the paragraph beginning at page 16, line 16 with the following replacement paragraph.

Another DNA which encodes a receptor of the invention is one having a contiguous nucleotide sequence substantially the same as:

nucleotides 71-1609 of Sequence ID No. 1 (which encodes a precursor-form of a mouse activin receptor);

variations of nucleotides 71-1609 of Sequence ID No. 15 1, wherein the codon for residue number 39 of the encoded amino acid codes for lysine, the codon for residue number 92 of the encoded amino acid codes for valine, and the codon for residue number 288 of the encoded amino acid encodes glutamine (which encodes a precursorform of a human activin receptor);

nucleotides 468-1997 of Sequence ID No. 3 (which encodes a precursor form of a Xenopus activin receptor); or

nucleotides 72-1550 of Sequence ID No. 11 (which encodes a precursor form of a rat activin receptor); or

variations of any of the above sequences which encode the same amino acid sequences, but employ different codons for some of the amino acids. --

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Please replace the paragraph beginning at page 17, line 1 with the following replacement paragraph.

Yet another DNA which encodes the above-described receptor is one having a contiguous nucleotide sequence substantially the same as set forth in Sequence ID No. 1, Sequence ID No. 15 4, Sequence ID No. 3, or Sequence ID No. 11

Please replace the paragraph beginning at page 37, line 23 with the following replacement paragraph.

receptor was identified (Sequence ID No. <u>15</u> ±). Due to the high degree of homology between this receptor and the mouse activin receptor, this receptor is designated as the human form of the activin receptor from the same subclass as the mouse receptor described above.

Please replace the paragraph beginning at page 43, line 7 with the following replacement paragraph.

Sequence ID No. 15 11 is a nucleic acid sequence encoding a humanderived activin receptor of the present invention. Sequence ID No. 15 11 is substantially the same as Sequence ID No. 1, except that the codon for amino acid residue number 39 encodes lysine (i.e., nucleotides 185-187 are AAA or AAG), the codon for amino acid residue 92 encodes valine (i.e., nucleotides 344-346 are GTN, wherein N is A, C, G or T), and the codon for amino acid residue number 288 encodes glutamine (i.e., nucleotides 932-934 are CAA or CAG).

10 N

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Please replace the paragraph beginning at page 43, line 22 with the following replacement paragraph.

Sequence ID No. 16 2¹ is an amino acid sequence for a human-derived activin receptor of the present invention. Sequence ID No. 16 2² is substantially the same as Sequence ID No. 2, except that amino acid residue number 39 is lysine, amino acid residue 92 is valine, and amino acid residue number 288 is glutamine —